Primary Prevention of Type-2 Diabetes in Developing Countries

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Although diabetes is now a worldwide epidemic, the rate of increase in its prevalence in developing countries is alarming. By the year 2025, more than three-quarters of all persons with diabetes will reside in developing countries. India and China are leading this surge in diabetes, and sub-Saharan Africa is currently at a lower prevalence rate. However, the estimated increase is substantial among African descendants in the Americas, West Indies and throughout the diaspora. There are compelling reasons why aggressive efforts must be directed toward primary prevention of diabetes in developing countries. Once diabetes develops, the cost of caring for patients is prohibitive. Poorly managed diabetes leads to several complications (e.g., end-stage renal failure, blindness, amputation and heart disease) that many developing countries are ill equipped to tackle. In landmark trials, lifestyle modification approaches are more efficacious than expensive medications in the prevention of diabetes. This is fortunate because lifestyle modification can be implemented locally, whereas medications often need to be imported at high cost. The first task is the education of policymakers on the urgent need for timely action to prevent the looming epidemic of diabetes. Once governments become convinced of its critical value, the translation of diabetes prevention through dietary modification and increased physical activity would require careful planning, extensive piloting and creativity in the allocation of scant resources. External support, foreign aid, debt forgiveness and other forms of creative financing will almost certainly be needed to implement widespread diabetes prevention programs in developing countries.

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Classification and Pathophysiology of Diabetes

Most cases of diabetes fall into one of two categories, although overlap may occur and the distinction may not always be clear.[1] Type-1 diabetes accounts for <10% of all cases of diabetes, tends to occur in younger subjects and is caused by severe insulin deficiency. The latter results from autoimmune destruction of the insulin-secreting beta cells of the pancreas. Type-2 diabetes, the predominant expression of the disease, is usually seen in older adults but is being diagnosed with increasing frequency in younger age groups, including children and adolescents.[2]

Obesity and physical inactivity are major risk factors[3] for type-2 diabetes in adults, adolescents and children (Table 1). Obesity, especially visceral obesity, induces insulin resistance, which predisposes to type-2 diabetes in genetically susceptible individuals. Insulin resistance and pancreatic islet beta-cell defect (leading to relative insulin deficiency) are the characteristic pathophysiologic findings in type-2 diabetes.[4] The etiology of the insulin secretory defect in type-2 diabetes is not well understood, but genetic factors probably are involved.[5]

Worldwide Epidemic of Type-2 Diabetes

Type-1 diabetes is predominantly a disease of persons of European ancestry and is much less prevalent among persons of African, Asian and other non-European descent, whereas type-2 diabetes is disproportionately more prevalent in non-European than European populations.[6] Because type-2 diabetes accounts for >90% of all cases of diabetes worldwide, the current diabetes epidemic is attributable predominantly to rising cases of type-2 diabetes. It has been estimated that the worldwide prevalence of diabetes in adults will increase to 300 million persons (5.4%) by the year 2025.[7]

Currently, diabetes is still more prevalent in developed than in developing countries (with

notable exceptions, such as the Pima Indians and Pacific Islanders of Kiribati, Nauru and other high-risk groups). However, the major part of the predicted increase will occur in developing countries. For example, over the period 1995–2025, the diabetes burden will increase from 51–72 million in the developed countries (an increase of 42%) but the projected increase in the developing countries will be from 84–228 million (170%). Thus, by the year 2025, more than three-quarters of all persons with diabetes will reside in developing countries.[6] India and China are leading this surge in diabetes, and sub-Saharan Africa is following with a much lower prevalence rate, at this time.

The faster rate of increase in the prevalence of type-2 diabetes in developing countries may relate to the effect of westernization superimposed on latent genetic predisposition to diabetes. Studies where persons from nonwestern traditional cultures are relocated to westernized environments have reported marked escalation in the risks for obesity and diabetes. A greater burden of insulin resistance also has been reported among persons from non-European populations compared with Europeans.[8-10]

Pattern of Diabetes in Developing Countries

Some unique aspects (Table 2) of the diabetes epidemic in developing countries include: 1) younger age group, 2) female gender preponderance, and 3) rural-to-urban area step-up in diabetes prevalence.[7] In developing countries, the majority of people with diabetes are in the age range of 45–64 years, as compared to aged ≥65 years in the developed countries. This demographic pattern will be amplified by the year 2025. Thus, diabetes in developing countries targets persons in the peak professional/productive years, whereas persons retired or nearing retirement age will be targeted in the developed world. The economic implications of this pattern are staggering. Moreover, the National Health and Nutrition Examination Survey (NHANES) 1999–2000 survey data showed a decreasing trend in age at diagnosis of diabetes for U.S. residents; a similar trend in developing countries will further magnify the problem of economic incapacitation by diabetes. In developed countries, there are more men than women with diabetes, whereas the gender ratios are reversed in developing countries.[7]

The combination of younger age and female preponderance increases the likelihood of intrauterine fetal exposure to diabetes in developing countries. Studies have indicated that exposure to an intrauterine diabetic environment increases the risk of developing future metabolic disorders.[11,12] Recent diabetes surveys in Jamaica, Barbados and other Caribbean islands confirm the same trends of younger age, female preponderance and rural-to-urban drift (Dr. Laurence Watkins, personal communication). In addition to these demographic patterns, the well-known complications of diabetes lead to predictably high morbidity and mortality in developing countries.[13,14]

Rationale for Aggressive Diabetes Prevention in Developing Countries

There are compelling reasons why primary prevention of type-2 diabetes should be the dominant strategy for developing countries. These include the prohibitive costs of treating established diabetes and multiple socioeconomic gaps in developing countries that predict poor outcome of diabetes management. There are gaps in health and social infrastructure, as well as health literacy. Then there are competing national priorities that relegate glycemic control in diabetic persons to second-tier concerns.

Prohibitive Costs of Glucose Control

Once diabetes has developed, it is expensive to treat because of the costs associated with routine medications, endless clinic visits, laboratory testing, supplies for home glucose monitoring, and treatment of complications. Local manufacture of drugs and devices used in the management of diabetes is nonexistent or limited in most countries of the developing world. This handicap makes for insecure availability of antidiabetes medications, including insulin, in local drug stores; frequent life-threatening shortages of insulin are not unusual in some poorer countries. Even when available, these medications often are unaffordable: one vial of the least expensive brand of insulin costs 5–10% of average annual income in Africa.[15] Costs of diabetes medications and medical supplies are not underwritten by government or reimbursed by third-party insurers in many such countries.

Many of the core paradigms of optimal diabetes management, including self-monitoring of blood glucose (SMBG) and routine measurement of hemoglobin A1c (HbA1c), are not feasible in poorer countries. In such countries, the majority of diabetes patients, because of economic constraints, cannot implement SMBG. Similarly, HbA1c, the "gold standard"

Table 1. Risk factors for type-2 diabetes

Nonmodifiable	Modifiable	Possibly Modifiable
Family history	Obesity/weight gain	History of hypertension
Racial/ethnic origin	Physical inactivity	History of dyslipidemia
Older age	Overeating	

test for evaluating glycemic control, is not available in most hospital laboratories due to lack of reagents, and many patients cannot afford routine measurement in a private laboratory. Tragically, the lack of day-to-day (SMBG) or long-term (HbA1c) feedback information on glycemic trends renders the state of diabetes control unknowable in most patients. As a result of inadequate healthcare infrastructure and socioeconomic limitations, the degree of glycemic control[16] necessary to prevent blindness, renal failure, amputation and heart disease may be beyond reach for patients in many developing countries. Therefore, poor glycemic control is pervasive, and the complications of diabetes are almost inevitable.

Exorbitant Costs of Managing Diabetes Complications

The complications of diabetes are rife among patients in developing countries.[13,14] Ironically, many of these countries lack the wherewithal for adequate management of target-organ dysfunction. In most of sub-Saharan Africa, renal replacement therapy (either chronic dialysis or transplantation services), laser surgery for retinopathy, invasive cardiology and coronary rescue procedures are not routinely available, even in tertiary care centers. Limb amputation, however, is available and performed frequently on patients with gangrenous diabetic foot ulcers.[13] Once the lower extremity has been amputated in a patient with diabetes in poorer countries, the economic contribution of that patient virtually ceases, because of poorly developed prosthetic and rehabilitation services.[11,12] Under such a grim scenario, a stronger case cannot be made for an aggressive focus on diabetes prevention as a top national priority in every developing country.

Strategies for Primary Prevention of Type-2 Diabetes

Developing countries besieged by other existential priorities have so far not focused on diabetes prevention. [The few local examples, such as the Tanzanian World Health Organization InterHealth Project, need to be replicated and expanded considerably.] The looming diabetes pandemic mandates that timely action be taken to place diabetes prevention as a top national priority in the developing world. The situation is somewhat reminiscent of (but far more hopeful than) that of HIV/AIDS.[17] A curious disorder, later characterized as HIV, emerged in the early 1980s. Despite a rapid growth in the understanding of the modes of transmission of HIV, little was done by way of preemptive community mobilization in Africa and Asia until two decades later, after the disease had afflicted and decimated large segments of the population in these regions. Developing countries currently have lower prevalence rates for type-2 diabetes than do developed countries, but the rate of increase is disproportionately greater among developing countries. As argued by Dr. King[7] of the World Health Organization (WHO), "worldwide surveillance of diabetes is a necessary first step toward its prevention ... which is now recognized as an urgent priority."

Preventive Interventions

In several large studies (Table 3), nonpharmacological approaches that focused on increased physical activity, reduction in caloric intake and modest weight loss have proved more efficacious in preventing type-2 diabetes than medications.[18-20] Therefore, these approaches must be considered the interventions of choice for the prevention of type-2 diabetes, particularly in the developing world.

The lifestyle intervention goal of the Diabetes Prevention Program (DPP)[20] was to achieve and maintain a weight reduction of ≥7% of initial body weight through modest caloric restriction (500–700 fewer calories per day) and physical activity of moderate intensity, such as brisk walking, for ≥150 minutes per week. The study subjects, all of whom had impaired glucose tolerance (IGT) at baseline, met with case managers one-to-one as well as in group sessions at frequent intervals. After an average follow-up period of 2.8 years, the incidence of diabetes was reduced by 58% in the lifestyle intervention group compared with placebo.[20]

The beneficial effect of lifestyle intervention was seen in all age, gender, racial and ethnic subgroups of the DPP participants. Furthermore, reversion to normal glucose tolerance occurred in ~30% of subjects in the lifestyle intervention arm, as compared with ~18% in the placebo arm. Thus, caloric restriction and increased physical activity not only prevented progression from IGT to diabetes but were also effective in restoring normal glucose tolerance in a substantial proportion of subjects with initial IGT.[20]

Table 2. Features of type-2 diabetes by world region*

	Developed Countries	Developing Countries
Number of cases (1995)	51 million	84 million
Projected cases (2025)	72 million	228 million
Rate of increase	42%	170%
Gender	Male > Female	Female > Male
Peak age	>65 years	45–64 years

* Data from King H, Aubert RE, Herman WH, 1998[7]

Translation of DPP Results in Developing Countries

The first task is the education of policymakers on the urgent need for action to prevent the looming epidemic of diabetes (Table 4). The WHO, practicing physicians, healthcare workers, civic organizations and academia should take the lead in this regard. Local diabetes organizations[21] could be a rallying point for sensitizing governments to the importance of diabetes prevention. Once governments become convinced of its critical value, the translation of diabetes prevention through dietary modification and increased physical activity could be easier than anticipated in developing countries.

The central control of policy and polity in many developing countries may actually facilitate the dissemination of healthy propaganda. The ministries of health, information, agriculture and education in these countries can rapidly implement public education and nutritional programs centered around the theme of diabetes prevention. The role of ministries of education in the maintenance and expansion of existing physical education programs in schools cannot be overemphasized. Similarly, the initiation and dissemination of national nutritional guidelines (currently a rarity in the developing world) by ministries of agriculture and health, in collaboration with appropriate experts, would be integral to the overall translation process.

To be successful, such programs must utilize culturally congruent methods for prevention of type-2 diabetes. With regard to the latter, pilot programs will be needed to validate the results of the published studies[18-20] in several locations on the African continent, the West Indies, Asia, Pacific rim, South America and other developing regions. Relatives of persons with diabetes would seem an obvious initial target for enrollment in local pilot studies. The purpose of such studies would be to identify culturally and regionally specific approaches (and constraints) to the translation of the key elements of the lifestyle arm of the DPP, including a determination of the feasibility of and best models for the delivery of physical activity and dietary interventions. Following the conclusion of local pilot programs, full implementation of diabetes prevention programs can be attempted in the general population. A phased approach with "waves" of centers spreading outwards from a core group of metropolitan diabetes prevention centers is an appealing strategy.

Cost of Diabetes Prevention

The costs associated with societal translation of diabetes prevention could be substantial. Analysis of costs associated with the DPP indicate that diabetes prevention did not come cheap, although the overall expense to society was cost-effective.[22,23] Over three years, the direct medical costs of the DPP interventions were $79 per participant in the placebo group, $2,542 in the metformin group and $2,780 in the lifestyle group.[22] One of the challenges in sub-Saharan Africa will be for the communities to develop their own brand of diabetes prevention interventions at an affordable cost. Reduction in contact frequency and size of personnel would lead to substantially lower costs. However, the minimum effective frequency of interaction and the optimal size of lifestyle interventionists need to be determined for

Table 3. Landmark diabetes prevention studies

Study	N	Mean Age (Years)	Mean BMI*	Ethnicity	Mean Follow-Up (Years)	Intervention	Diabetes Reduction** (%)
Da Qing[18]	577	45	26	Chinese	6	Diet + exercise	33–47%
Finnish[19]	522	55	31	European	3.2	Diet + exercise	58%
DPP[20]***	3,234	50.6	34	Multiethnic	2.8	Diet + exercise	58%
						Metformin	31%

* BMI: body mass index; ** Percentage reduction in incidence of diabetes compared with control; *** DPP: Diabetes Prevention Program

Table 4. Approach to translation of diabetes prevention in developing countries

- Initial education of national and local policymakers on the need for primary prevention of diabetes
- Collaboration among ministries of health, information, education, agriculture and other stakeholders
- Incorporation of diabetes prevention information in school curriculum at elementary, secondary and higher levels
- Maintenance and expansion of existing physical education programs in schools
- Initiation and dissemination of national nutritional guidelines
- Involvement of healthcare community and civic organizations
- Formal launching of local pilot and feasibility programs on diabetes prevention
- Centrifugal spread of local diabetes prevention centers from metropolitan to rural areas

each community. Indeed, this information should be the focus of the pilot and feasibility studies in the various communities.

Clearly, the adaptation of diabetes prevention programs to developing countries would require creativity in fundraising, cost containment, and cost-sharing. Savings from cutting personnel and visits to local diabetes prevention centers may need to be ploughed back into the development of infrastructure for expansion of the program to wider segments of society. Realistically, the sparse gross domestic product for most developing countries predicts that even a minimally effective society-wide diabetes prevention program may be unaffordable. Therefore, external funding would be critical for the initiation and maintenance of local diabetes prevention programs. Foreign aid and grants from international philanthropic sources and nongovernmental organizations can be structured for specific health-related outcomes.

Finally, debt-forgiveness programs in which the wealthy Group-of-Eight (G8) countries liquidate or commute debts owed to them by poorer nations can (and should) be linked to specific socioeconomic, political and health outcomes, in a paradigm that rewards poorer countries for excellence in the development and execution of programs in the aforementioned areas. There is already a precedent for debt forgiveness in the context of spreading democracy to societies emerging from dictatorial regimes. A clear and compelling case exists for extending the same consideration to developing nations, especially in sub-Saharan Africa, where debt forgiveness can become a potent foreign policy tool that drives national health policies and practices. It is envisioned that the proportion of debt forgiven can somehow be linked to demonstrable efforts in the areas of disease prevention and health promotion in diabetes and other specific areas (e.g., childhood immunization, HIV-AIDS awareness and prevention, etc.).

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